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AWARD NUMBER: W81XWH-06-1-0245

TITLE: Contribution of AMACR and Phytanic Acid to Prostate Cancer Risk Among African Americans in North Carolina

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REPORT DATE: May 2009

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
1 May 2009	Final	15 Jan 2006 – 14 Apr 2009

4. TITLE AND SUBTITLE

Contribution of AMACR and Phytanic Acid to Prostate Cancer Risk Among African Americans in North Carolina

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-06-1-0245

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Wake Forest University Health Sciences
Winston-Salem, NC 27157

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Several lines of evidence have suggested genetic and dietary differences may be important in PCa, particularly among AA (African American) men. In this study, we aimed to test the hypothesis that mutations/sequence variants in the AMACR gene, and dietary intake of foods rich in phytanic acid, increase the risk to PCa among AA men. We conducted a population based study by ascertaining 213 AA men who have PCa and 264 race, age, and county-matched controls from 15 counties of North Carolina. We have completed the 1st task, study subject recruitment. We have also obtained additional grant funding related to the science of this project, which will help provide independent confirmation of the findings from this study in a different study population. We have used the newly recruited study population to complete a study confirming genome-wide variants in AA PCa cases and controls, and our results are in-press. The results from this project have increased our knowledge of potential risk factors and suggest potential preventive strategies for prostate cancer in AA men.

15. SUBJECT TERMS
Prostate Cancer, Phytanic Acid, AMACR, African American, Susceptibility, Association

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU		19b. TELEPHONE NUMBER *(include area code)*

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Introduction

Several lines of evidence have suggested genetic and dietary differences may be important in PCa, particularly among AA men. Specifically, the *AMACR* gene has been implicated by gene expression profiling of tumors, as well as in genetic studies among mostly Caucasian American subjects. Additionally, the *AMACR* gene happens to be required for the metabolism of phytanic acid, which is obtained in the human diet almost exclusively in red meat and dairy products, both of which have been implicated in PCa risk. In this study, our primary goal is to test the hypothesis that mutations/sequence variants in the *AMACR* gene increase the risk to PCa among AA men. Our secondary goal is to test the hypothesis that PCa risk is increased by dietary intake of foods rich in phytanic acid, and that this risk is further increased due to alterations in *AMACR*. To test these hypotheses, we conducted a population based study by ascertaining a total of 518 AA men. Our primary aim is to identify the AA spectrum of mutations and sequence variants in AMACR and assess their contribution to PCa. Our secondary aim is to preliminarily assess the contribution to PCa risk related to dietary intake of foods rich in phytanic acid, and then explore the interaction effect between AMACR and phytanic acid.

Body

Summary from previous reports

We spent the first 8 months (Jan-Aug 2006) of the funding period working to obtain regulatory approval from the IRB of the USAMRMC (DOD). We then spent two months (Sept-Oct 2006) obtaining approval from the North Carolina Cancer Registry Committee and our local IRB at Wake Forest University School of Medicine, thus allowing us to begin recruitment. The cancer registry began identification of cases for our study in early November 2006, and then reported the first batch of cases to us in late November. We began to recruit subjects in early December 2006.

Because of the late start in subject recruitment, we worked with the North Carolina Central Cancer Registry to expand our study area from 7 counties to a total of

15 counties, effective October 2007. In addition, we worked with the DoD to obtain a three month extension of the study, at no additional cost.

The specific accomplishments associated with each task in the Statement of work are detailed in the following section.

Summary for current final report

We have recruited a population based sample of 233 AA men who have PCa and 285 race, age, and county-matched controls from 15 counties of North Carolina, for a total of 518 AA men. Our primary aim has been completed, and our secondary aim is nearly complete. We have generated important findings from the samples and data collected from this study population, and have already worked to ensure that this study makes a continued contribution to the fight against PCa.

Statement of Work

Task 1. To recruit 250 AA men who have PCa and 250 race, age, and county-matched controls from eight counties of North Carolina, in a population based study. These can be combined with our pilot study population, for a total of ~550 AA men.

1. We have recruited a population based sample of 233 AA men who have PCa and 285 race, age, and county-matched controls from 15 counties of North Carolina.
2. The total of 518 subjects is slightly short of our goal. However, we exceeded our recruitment goals for control subjects, and we also expect to use institutional support to recruit a few more lingering cases after the official end of our funding period. In addition, the number of subjects that we have already ascertained is sufficient to allow us to conduct important research.
3. We plan to continue to expand this study population via other funding mechanisms, and we are in the process of drafting follow-up grants.
4. We have already initiated additional work above and beyond what we originally proposed. To realize the full potential of our recruitment efforts, we participate in consortia with other institutions that are interested in the study

of PCa among AA men. First, we lead a mini-consortium of AA study populations totaling approximately 867 PCa cases and 880 controls, consisting of Johns Hopkins (Baltimore, Maryland), Washington University (St. Louis, Missouri), and another investigator at Wake Forest (Winston-Salem, North Carolina). Second, we have joined a larger consortium, named MADCAP, which is a nationwide collaborative effort to bring together all available AA study populations. By actively participating in these two consortiums, we help to ensure the samples and data we have collected will have the greatest possible impact in the fight against PCa.

Task 2. To identify sequence variant/mutation spectrum of the AMACR gene in AA men.

1. We used the HapMap database (http://www.hapmap.org/) to identify tagging SNPs (tSNPs) in the AMACR gene. Based on Pair-wise tagging, we selected 27 tSNPs in total, in order to tag 52 SNPs, with MAF >5% and rsq>0.8. The AMACR gene spans slightly more than 20kb, and our selected tSNPs will cover 5kb beyond 5'-end and 2kb beyond 3'-end of AMACR transcript. See table 1 for a listing of the selected tSNPs.

Table 1. Association study of AMACR gene(34,023,663 - 34,043,963) in African-American population

CHR	SNP	BP	m/M
5	rs13289	34,022,166	C/G
5	rs16892064	34,023,885	T/C
5	rs6898962	34,023,992	T/C
5	rs6863560	34,024,728	G/T
5	rs2278008	34,025,275	G/A
5	rs10472908	34,025,912	G/C
5	rs250414	34,026,380	A/G
5	rs3822464	34,026,893	G/A
5	rs2652130	34,027,156	G/T
5	rs16892090	34,028,645	T/A
5	rs10472909	34,029,873	A/T
5	rs16892096	34,029,939	G/A
5	rs253190	34,030,621	T/C
5	rs168803	34,031,462	G/T
5	rs34676	34,033,748	T/G
5	rs16892121	34,034,151	G/C
5	rs2287939	34,034,640	T/C
5	rs34679	34,035,814	T/C
5	rs34682	34,037,201	G/T
5	rs39663	34,037,711	T/C
5	rs7713302	34,038,592	T/C
5	rs34683	34,038,940	C/G
5	rs7733150	34,040,648	A/T
5	rs16892145	34,041,010	T/G
5	rs34687	34,042,267	A/G
5	rs253198	34,046,396	G/A
5	rs1423674	34,047,518	G/A

Task 3. To genotype mutations/sequence variants in AMACR among AA men and evaluate their contribution to and association with PCa

1. We genotyped 27 SNPs in the AMACR gene region. Three SNPs (rs250414, rs10472909, rs16892096) reached statistical significance ($p<0.05$). The minor alleles of rs250414 (OR=0.7) and rs10472909 (OR=0.74) were each

associated with a decreased risk, while the minor allele of rs16892096 (OR=1.81) was associated with an increased risk for prostate cancer.

Table 2. Association study of AMACR gene(34,023,663 - 34,043,963) in African-American population

		NC study centers(case = 172, control = 248)			
CHR	SNP	MAF_Case	MAF_Ctnl	P†	OR(95% CI)*
5	rs13289	0.372	0.357	0.704	0.94(0.70-1.28)
5	rs16892064	0.061	0.058	0.645	1.16(0.61-2.21)
5	rs6898962	0.143	0.147	0.979	1.01(0.67-1.50)
5	rs6863560	0.270	0.275	0.852	0.97(0.70-1.34)
5	rs2278008	0.236	0.204	0.235	1.24(0.87-1.76)
5	rs10472908	0.126	0.091	0.128	1.46(0.90-2.36)
5	rs250414	0.230	0.270	0.049	0.7(0.49-1.00)
5	rs3822464	0.298	0.349	0.092	0.77(0.57-1.04)
5	rs2652130	0.267	0.220	0.139	1.30(0.92-1.83)
5	rs16892090	0.181	0.218	0.444	0.87(0.60-1.25)
5	rs10472909	0.448	0.526	0.045	0.74(0.55-0.99)
5	rs16892096	0.102	0.063	0.033	1.81(1.05-3.14)
5	rs253190	0.285	0.268	0.391	1.15(0.83-1.60)
5	rs168803	0.288	0.244	0.194	1.25(0.89-1.76)
5	rs34676	0.488	0.462	0.977	1.01(0.74-1.36)
5	rs16892121	0.073	0.079	0.925	0.97(0.56-1.70)
5	rs2287939	0.189	0.151	0.238	1.27(0.85-1.89)
5	rs34679	0.444	0.468	0.989	1.00(0.74-1.35)
5	rs34682	0.125	0.149	0.346	0.81(0.53-1.25)
5	rs39663	0.076	0.073	0.815	1.07(0.61-1.89)
5	rs7713302	0.265	0.274	0.718	1.06(0.77-1.47)
5	rs34683	0.128	0.131	0.807	1.06(0.67-1.66)
5	rs7733150	0.038	0.043	0.840	0.92(0.43-1.99)
5	rs16892145	0.111	0.107	0.670	1.11(0.69-1.78)
5	rs34687	0.462	0.456	0.244	1.19(0.89-1.60)
5	rs253198	0.192	0.173	0.369	1.20(0.81-1.77)
5	rs1423674	0.308	0.316	0.545	1.10(0.80-1.52)

† P-values were calculated adjusted for age and ancestry proportion.

2. To confirm and strengthen our findings, we also evaluated these same 27 SNPs in our mini-consortium of AA men (see mini-consortium description above for Task 1, number 4). In this confirmation study population, three SNPs (rs34676, rs16892121, and rs34687) reached statistical significance ($p<0.05$), although these did not include any of the three observed as

significant in our new NC study population. However, one SNP (rs10472909) was confirmed as marginally significant, and in the same direction of association.

Table 3. Association study of AMACR gene(34,023,663 - 34,043,963) in African-American population

		Non-NC study centers(case = 695, control = 632)				All study centers(case = 867, control = 880)			
CHR	SNP	MAF_Case	MAF_Ctnl	P‡	OR(95% CI)*	MAF_Case	MAF_Ctnl	P‡	OR(95% CI)*
5	rs13289	0.338	0.346	0.557	0.95(0.80-1.13)	0.345	0.349	0.678	0.97(0.84-1.12)
5	rs16892064	0.069	0.076	0.461	0.89(0.65-1.21)	0.067	0.071	0.571	0.92(0.70-1.22)
5	rs6898962	0.145	0.151	0.609	0.94(0.75-1.18)	0.145	0.150	0.667	0.96(0.79-1.16)
5	rs6863560	0.267	0.247	0.244	1.12(0.93-1.34)	0.267	0.255	0.402	1.07(0.91-1.26)
5	rs2278008	0.220	0.229	0.729	0.97(0.80-1.17)	0.223	0.222	0.750	1.03(0.87-1.21)
5	rs10472908	0.122	0.141	0.229	0.86(0.68-1.10)	0.123	0.126	0.841	0.98(0.79-1.21)
5	rs250414	0.244	0.241	0.735	0.97(0.80-1.17)	0.241	0.249	0.345	0.92(0.78-1.09)
5	rs3822464	0.321	0.337	0.131	0.88(0.75-1.04)	0.317	0.341	0.043	0.87(0.75-1.00)
5	rs2652130	0.233	0.222	0.321	1.10(0.91-1.33)	0.240	0.221	0.134	1.13(0.96-1.34)
5	rs16892090	0.184	0.192	0.774	0.97(0.79-1.19)	0.183	0.199	0.415	0.93(0.78-1.11)
5	rs10472909	0.468	0.498	0.068	0.86(0.73-1.01)	0.464	0.506	0.009	0.83(0.72-0.95)
5	rs16892096	0.081	0.081	0.743	1.05(0.79-1.40)	0.085	0.076	0.215	1.17(0.91-1.51)
5	rs253190	0.241	0.240	0.720	1.03(0.86-1.24)	0.249	0.248	0.560	1.05(0.90-1.23)
5	rs168803	0.290	0.302	0.288	0.91(0.76-1.08)	0.290	0.286	0.845	0.98(0.84-1.15)
5	rs34676	0.501	0.477	0.039	1.19(1.01-1.40)	0.503	0.494	0.154	1.11(0.96-1.28)
5	rs16892121	0.088	0.066	0.009	1.51(1.11-2.07)	0.085	0.069	0.032	1.34(1.03-1.74)
5	rs2287939	0.199	0.215	0.243	0.89(0.73-1.08)	0.197	0.197	0.731	0.97(0.81-1.16)
5	rs34679	0.411	0.408	0.545	1.05(0.89-1.24)	0.417	0.425	0.842	1.02(0.88-1.17)
5	rs34682	0.120	0.122	0.971	1.00(0.78-1.28)	0.121	0.129	0.531	0.93(0.76-1.15)
5	rs39663	0.067	0.070	0.685	0.94(0.68-1.28)	0.069	0.071	0.759	0.96(0.73-1.26)
5	rs7713302	0.249	0.246	0.738	1.03(0.86-1.25)	0.252	0.254	0.827	1.02(0.87-1.20)
5	rs34683	0.143	0.130	0.234	1.15(0.91-1.46)	0.140	0.130	0.324	1.11(0.90-1.36)
5	rs7733150	0.052	0.049	0.391	1.18(0.81-1.71)	0.049	0.048	0.557	1.10(0.79-1.54)
5	rs16892145	0.095	0.094	0.906	1.02(0.77-1.34)	0.098	0.098	0.781	1.03(0.82-1.31)
5	rs34687	0.452	0.423	0.041	1.19(1.01-1.40)	0.454	0.432	0.050	1.15(1.00-1.33)
5	rs253198	0.192	0.166	0.080	1.21(0.98-1.49)	0.192	0.168	0.061	1.19(0.99-1.43)
5	rs1423674	0.287	0.281	0.506	1.06(0.89-1.27)	0.291	0.291	0.605	1.04(0.89-1.22)

‡ P-values were calculated adjusted for age, ancestry proportion, and study centers.

* Odds ratio(OR) is calculated for minor allele(m). In non-NC centers, rs34676 has minor allele = G.

3. Importantly, when we combined all of the data for our new NC study population and the mini consortium, rs10472909 stands out as highly significant (p=0.009), and with a consistent direction of association across all study populations (minor allele associated with decreased risk).
4. In addition to investigating the association between AMACR tSNPs and PCa risk, we recently genotyped a newly identified germline deletion polymorphism located in the AMACR promoter CpG island (Zhang 2009). This deletion polymorphism has relatively high frequency (43%) in a general population and has been shown to be associated with tumor differentiation in colon cancers (Zhang 2009). We hypothesized that germline deletion polymorphism in the AMACR promoter CpG island also affect PCa

differentiation and may have prognostic value for disease progression. Data analysis for this sub-project is in progress.

5. In addition to our study of the AMACR gene, we have used this newly recruited study population to complete a study aimed at confirming results from previous publications of genome-wide association studies (GWAS). All of the prior publications on these variants had been limited to Caucasian subjects, so our paper in AA PCa cases and controls, and is an important step towards addressing the understudied problem of increased prostate cancer risk among AA men. Table 4 summarizes our results, which are in-press.

Table 4. Summary results of prostate cancer association in African Americans

				Risk	Combined (860 ca/853 co)				WFU_NC (164 ca/221 co)			
CHR	SNP	BP	Alleles	allele	*P*-CMH	OR	L95	U95	Case	Cont	*P*-allele	OR
2p15	rs721048	63,043,382	A/G	A	**0.03656**	1.40	1.02	1.91	0.110	0.066	0.03	1.756
3p12	rs2660753	87,193,364	T/C	T	0.2332	1.09	0.95	1.25	0.420	0.470	0.18	0.82
6q25	rs9364554	160,804,075	T/C	T	0.8378	1.03	0.78	1.36	0.095	0.097	0.90	0.969
7p15 (JAZF1)	rs10486567	27,749,803	T/C	C	0.1363	0.89	0.76	1.04	0.744	0.749	0.88	1.027
7q21 (LMTK2)	rs6465657	97,460,978	T/C	C	0.5734	1.06	0.87	1.29	0.811	0.817	0.84	1.039
8q24 (Kittle)	rs7008482	126,336,812	T/G	G	0.9463	0.99	0.82	1.20	0.759	0.801	0.17	1.275
8q24 (Kittle)	rs2124036	126,717,316	T/C	C	0.9434	1.01	0.85	1.19	0.686	0.738	0.12	1.287
8q24 (Kittle)	rs780321	127,152,877	C/T	T	0.4784	0.95	0.81	1.10	0.653	0.690	0.28	1.181
8q24 (JHH)	rs10086908	128,081,119	C/T	T	**0.00237**	0.77	0.66	0.91	0.745	0.738	0.81	0.96
8q24 (JHH)	rs6981122	128,163,642	A/C	C	**0.00753**	0.81	0.70	0.95	0.682	0.710	0.40	1.143
8q24 (2)	rs16901979	128,194,098	A/C	A	**0.0056**	1.22	1.06	1.41	0.451	0.419	0.37	1.142
8q24 (3)	rs6983267	128,482,487	T/G	G	0.7739	0.97	0.77	1.22	0.838	0.864	0.32	1.227
8q24 (1)	rs1447295	128,554,220	A/C	A	0.9779	1.00	0.86	1.16	0.293	0.330	0.27	0.839
9q33 (DAB2IP)	rs1571801	121,506,927	T/G	T	0.1514	1.16	0.95	1.41	0.190	0.149	0.13	1.338
10q11 (MSMB)	rs10993994	51,219,502	T/C	T	0.465	0.95	0.82	1.09	0.585	0.591	0.89	1.021
10q26 (CTBP2)	rs4962416	126,686,862	G/A	G	0.4501	1.07	0.89	1.29	0.177	0.177	0.99	1.002
11q13 (2)	rs12418451	68,691,995	A/G	A	0.7443	0.97	0.79	1.19	0.146	0.179	0.23	0.788
11q13 (1)	rs10896449	68,751,243	A/G	G	0.9618	1.00	0.86	1.16	0.657	0.661	0.93	1.014
17q12 (2) (HNF1B)	rs11649743	33,149,092	T/C	C	0.6283	0.93	0.70	1.24	0.909	0.928	0.34	1.29
17q12 (1) (HNF1B)	rs4430796	33,172,153	T/C	T	**0.02507**	1.18	1.02	1.37	0.354	0.344	0.78	1.044
19q13	rs887391	46,677,464	C/T	G	0.2698	0.92	0.80	1.06	0.438	0.505	0.07	0.766
19q13 (KLK3)	rs2735839	56,056,435	A/G	G	0.3248	1.08	0.93	1.26	0.695	0.674	0.54	0.908
22q13	rs9623117	38,776,619	T/C	C	0.697	0.97	0.83	1.14	0.674	0.706	0.34	1.162
Xp11	rs5945619*	51,074,708	G/A	G	0.4055	1.09	0.89	1.34	0.337	0.367	0.56	0.88

Task 4. To measure serum levels of phytanic acid and intake of dairy products and meat consumption for each subject, and test whether these levels increase the risk to PCa among AA men.

1. For all subjects enrolled in this study, we have completed questionnaire data entry for dietary intake of dairy products and meat consumption. This data is currently being analyzed.
2. We are still in the process of measuring serum levels of phytanic acid in our complete study population. However, in an initial subset of the data, we have observed that serum levels of PA correlate very well with dietary intake of foods that are rich in PA. Furthermore, we have obtained relevant results that will help drive our ongoing work in this area, as described in the following.
3. We obtained additional intramural funding from our institution for a similar study that is related to the science of this project. Phytanic Acid serum measurement in a Swedish population is currently being generated by the mass spec lab, and will be ready for analysis within 1 month. We have measured serum levels of phytanic acid in a Swedish study population. Eventually, the findings of this Swedish study population may be important for comparison and independent confirmation of our hypothesis.
4. We identified a collaborator at Virginia Tech whose lab measured phytanic acid levels in food items. These new results will greatly aid our ability to interpret the results of the dietary health questionnaires that we collected from each subject in our newly recruited AA study population. See table 5 below.

Table 5. Phytanic acid content of food samples

Food Product	Origin	Fat % w/w	Serving size	Units	Pool 1 mg/g fat	Pool 2 mg/g fat	Mean mg/g fat	Mean mg/100g or ml food	Mean mg/serving
Milk, Whole	Kroger whole milk	3.4	237	ml	4.3	4	4.15	14.1	33.3
Milk, 2%	Kroger 2% milk	2.1	237	ml	4.6	4.2	4.4	9.3	22.1
Milk, 1%	Kroger 1% milk	1.1	237	ml	6.1	5.8	5.95	6.3	0
Milk, skim	Kroger skim milk	0.4	237	ml	0	0	0	0	0
beverages	Ensure vanilla	3.6	237	ml	0	0	0	0	0
Ice cream, regular fat	Kroger cookies and cream	16.4	60	g	5.6	3.9	4.75	78	46.8
Sherbet	Kroger Lime	0	85	g	0	0	0	0	0
Ice cream, low fat	Light	2.7	72	g	5.6	5.6	5.6	15.1	15.1
Cream, regular	cream	33.3	15	ml	7.2	7.7	7.45	248.3	37.3
Cream, Half and half	Kroger Half and half	10	30	ml	7.8	8	7.9	79	23.7
Pudding	Hubnt's Caramel Cream	3	99	g	1.1	1.6	1.35	4.1	4.1
Frozen Yogurt	Country Club Peach	1.6	64	g	0	0	0	0	0
Yogurt, regular fat	Kroger Vanilla	1.8	227	g	4.3	2.7	3.5	6.2	14
Yogurt, low fat	Kroger Low Fat Vanilla	1.5	227	g	2.2	4.1	3.15	4.9	11
Yogurt, fat free	Kroger Fat Free Vanilla	0	227	g	0	0	0	0	0
regular fat	Kroger Large Curd	4	113	g	5.5	6.9	6.2	24.7	27.9
fat	Kroger Low Fat	2.5	113	g	4.9	6.6	5.75	14.4	16.2
free	Kroger Fat Free	0	113	g	0	0	0	0	0
fat	Wishbone Italian	26.7	30	ml	0	0	0	0	0
Salad dressing, low fat	Krant Light House Italian	10.9	32	ml	0	0	0	0	0
Free	Kraft Free Zesty Italian	0	32	ml	0	0	0	0	0
Cheese, regular fat	Kraft Cheddar	35.7	28	g	3.7	3	3.35	119.6	33.5
Cheese, low fat	Kraft Cheddar 2%	14.3	28	g	5.2	3.2	4.2	60	16.8
Cheese, fat free	Kraft slices fat free	0	21	g	0	0	0	0	0
Sour cream, regular fat	Breakstones	16.7	30	g	5.4	10	7.7	128.3	38.5
fat	Breakstones	9.7	31	g	6	7.4	6.7	64.8	20.1
Ricotta cheese	Kroger	9.7	62	g	3	2.7	2.85	27.6	17.1
Macaroni and cheese	Amy's frozen	2.3	256	g	0.9	1.6	1.25	2.9	7.5
Cream cheese	Philadelphia Original	32.1	28	g	1.9	1.7	1.8	57.8	16.2
Butter, regular	Kroger unsalted	78.6	14	g	3.3	2.8	3.05	239.6	33.6
Butter, light	Kroger light salted	42.9	14	g	4.6	2	3.3	141.4	19.8
Chocolate, milk	Nestle	2.1	240	ml	0.8	1.3	1.05	2.2	5.3
Chocolate, dark	Cadbury Royal Dark	30.8	39	g	0	0	0	0	0
Fish sticks, fried fish	Gortons Crunchy golden	11.1	108	g	3.1	3	3.05	33.9	36.6
fresh	Kroger	12.2	85	g	9	9.8	9.4	114.7	97.5
Salmon, canned	Double Q Wild Pink	2.4	63	g	8	8.6	8.3	19.8	12.5
Sardines	King Oscar in soybean oil	12.9	85	g	1.2	1.1	1.15	14.9	12.7
Mackeral	tomato sauce	3	110	g	1.6	1.9	1.75	5.3	5.8
Canned tuna	Star Kist albacore in water	3.6	56	g	1.2	1.6	1.4	5	2.8
Fish oil	Sundown 1000	100	1	g	4.2	3.6	3.9	390	3.9
Cod liver oil	Nature made	100	0.5	g	4.1	4.9	4.5	450	2.3
Beef Tallow	Wade's Supermarket	98.5	13	g	3.7	5	4.35	428.3	55.7
Ground beef	Kroger 75% lean	24.8	113	g	2.3	2.2	2.25	55.8	57.3
Beef Steak	Kroger Sirloin	7.1	85	g	1.9	1.9	1.9	13.4	11.4
Beef Pot Roast	Kroger blade pot roast	12.9	85	g	1.9	2	1.95	25.2	21.5
Stew beef	Kroger	5.4	85	g	3	1.7	2.35	12.7	10.8
Pot pie	Mushroom Chicken	14.1	234	g	0	0	0	0	0
Beef liver	Wade's Supermarket	8.2	85	g	0.9	1.6	1.25	10.3	8.8
Beef spare ribs	Wade's Supermarket	22.4	85	g	2.2	2.9	2.55	57	48.5
sandwiches	Land O'frost	4.4	57	g	0.7	0.7	0.7	3.1	1.75
Lunch meet bologna	Gwaltney	15.6	32	g	1.9	2.2	2.05	32	10.3
Lunch meat salami	Kroger Value	13.8	58	g	2	0.9	1.45	20	11.6
beef	Grace corned beef	14.3	56	g	2	1.6	1.8	25.7	14.4
Beef sausage	sausage	10.7	56	ml	0.7	0.7	0.7	7.5	4.2
Beef broth	Kroger beef broth	0.2	240	ml	0.7	0.7	0.7	0.15	0.35
Beef gravy	Campbell's	1.7	59.25	ml	0.2	0.2	0.2	0.3	0.2
Peanut butter	Kroger creamy	50	32	g	0	0	0	0	0
Cooked greens	Collard Greens Canned	0.5	190	g	0	0	0	0	0
Tomato juice	Campbell	0	240	ml	0	0	0	0	0

Key Research Accomplishments

- Significantly expanded the study population
- Comprehensively studied genetic variation in AMACR and association with PCa risk among AA men
- Utilized the study population in research that is directly and indirectly relevant to the original proposal
- Performed additional studies that enhance the impact of this project
    - Collaboration within our mini consortium
    - Collaboration with the MADCAP consortium

- Confirmation study of PCa GWAS variants for the first time in an AA population
- Measurement of phytanic acid levels in food items to improve the accuracy of dietary estimates

Reportable Outcomes

We completed all tasks associated with our primary Aim

1. We have recruited a new study population of AA men with PCa.
2. We have a paper in press that describes identification of a SNP (rs10472909) in the AMACR gene as the most consistently associated with prostate cancer risk. In addition, we identified several other SNPs in AMACR that may warrant additional follow-up.
3. We have used the newly recruited study population to complete two additional studies that are in-press. One is a study of a newly discovered deletion in the AMACR gene. The other is a study confirming variants, which had been identified in GWAS of CA subjects, among AA PCa cases and controls.

Despite delays in the beginning of this project, we made great progress toward completion of our secondary aim. We have entered all of the dietary questionnaire data and are in the process of analyzing the resulting data. Related to the secondary aim, we have measured phytanic acid levels in a variety of food items, enabling us to better interpret our dietary questionnaire data. We are in the process of measuring phytanic acid levels in serum samples from another study population consisting of Swedish men, soon to be followed by our newly recruited AA study population.

Conclusion

We have greatly expanded our AA study population, and have established collaborations. This will help improve our ability to learn why AA men are at the highest risk of PCa.

Despite delays in the beginning of the project, we completed almost all of the proposed laboratory and analytical work, and in several areas have expanded beyond what the originally proposed science. Several manuscripts are currently in development. In areas where we were unable to complete a proposed task, we made great strides both directly and indirectly related to the original proposal. As documented in previous semi-annual and annual reports, there were some delays in the project during the startup phase due to IRB and cancer registry delays; however, we have been able to overcome most of the delays and we have complete the primary tasks as proposed. In addition, we successfully handled a change in the PI toward the end of the study, which slightly delayed the final report.

We continue to look for opportunities for additional studies based on this study population, as shown by our GWAS confirmation study that is in-press, and in our work to collaborate with other groups.

The direct results from this study, as well as other future studies based on this study population, will greatly increase our knowledge of potential risk factors and suggest for potential preventive strategies for prostate cancer in AA men. These men have the highest risk to develop prostate cancer, and the highest risk to eventually develop aggressive forms of prostate cancer, while also being an understudied group. Therefore, this project fills a vital gap in our understanding of prostate cancer etiology. This study could potentially clarify the diet-gene interactions that lead to prostate cancer. Specifically, this project could lead to genetic testing that would help identify men with increased prostate cancer risk, while at the same time offering these men targeted guidance to reduce this risk by lowering their dietary intake of certain foods such as dairy, red meat, and fatty fish.

References.

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List of personnel receiving pay from the research effort.

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4. Mara Vitolins
5. Janet Tooze
6. Aubrey Turner
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